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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/736,868	12/16/2003	Aaron Solomon	NWESTERN-08451	9086

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EXAMINER

PRIEBE, SCOTT DAVID

ART UNIT	PAPER NUMBER
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1633

DATE MAILED: 07/28/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/736,868

Applicant(s)

SOLOMON ET AL.

Examiner

Scott D. Priebe, Ph.D.

Art Unit

1633

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 16 December 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-12 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-12 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 16 December 2003 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

S.O.V

DETAILED ACTION

Specification

The disclosure is objected to because of the following informalities: the term “*Steinermatidea*” and “*Heterorahbtidea*” (e.g. page 2, line 5, and page 3, line 4) are misspellings of *Steinernematidae* and *Heterorhabditidae*.

Appropriate correction is required.

Claim Objections

Claim 9 is objected to because of the following informalities: “*Steinermatidea*” and *Heterorahbtidea* are misspellings of *Steinernematidae* and *Heterorhabditidae*. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-12 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant

Art Unit: 1633

art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 1-11 are directed to compositions comprising “mutant nematodes altered to reduce or increase sensitivity to desiccation stress” and methods of treating a host organism with such compositions. Claim 2 limits the generic mutant nematode of the collection to one with a knock-out osmotic stress resistant mutation. All of the claims are directed to a generic mutant nematodes that have some generic alteration that either increases or decreases their sensitivity to desiccation stress. As indicated in the rejection under 35 U.S.C. 112, second paragraph, it is unclear if the alteration is the mutation or not. The only possible examples of the claimed nematodes described in the specification are mutants (decreased sensitivity) of wild-type *Caenorhabditis elegans* Bristol strain N2 that have a loss of function mutation in a previously unknown or uncharacterized gene that Applicant’s have named OSR-1 (page 80), and otherwise uncharacterized mutants *osr-2*, *osr-3*, and *osr-4*, and prior art mutants of N2 with *age-1* (decreased sensitivity) or *daf-16* (increased sensitivity) mutations. The specification indicates that mutations in an N2 background conferring decreased sensitivity to osmotic stress were distributed into four complementation groups, *osr-1* to *osr-4*, but does not provide any characteristics of *osr-2*, *osr-3*, and *osr-4* that would allow one to determine what they were. The specification discloses nucleotide coding sequence and amino acid sequence corresponding to OSR-1, but not for the three other complementation groups, and there is no indication that any of the *osr-2*, *osr-3*, and *osr-4* mutants were deposited.

The specification describes these mutations as affecting sensitivity to desiccation in general, which includes osmotic desiccation and evaporative desiccation. However, the evidence

Art Unit: 1633

presented in the specification shows only their susceptibility or resistance to hypertonic or hyper-osmotic stress (osmotic desiccation). These two forms of desiccation stress are not the same and the results of Piggot et al. (Nematol. 2(5): 561-566, 2000) show that the response of a nematode to these two forms of stress are not regulated the same. A mutant of *Heterorhabditis megidis* strain UK211 that has increased resistance to evaporative desiccation but was slightly sensitive to hyper-osmotic stress (page 564). There is no evidence of record that *osr-1*, *daf-16* or *age-1* mutants of N2 have either increased or decreased resistance to evaporative desiccation stress relative to wild-type N2, and thus, no evidence that Applicant was in possession of a single species of nematode with decreased sensitivity to evaporative desiccation, much less a genus of nematodes embracing such.

Even if the claims were limited to altered sensitivity to osmotic stress, the specification does not describe any nematodes other than *osr-1*, *daf-16* or *age-1* mutants of *C. elegans* that have altered sensitivity to osmotic stress, whereas the claims are directed to all nematodes, any mutation that confers increased or decreased sensitivity to osmotic stress, and possibly alterations that are not mutations (see rejection under 35 U.S.C. 112, second paragraph). With respect to OSR-1, a search of nucleic acid sequences in the prior art revealed only cosmid clones of genomic DNA from *C. elegans* and *C. briggsae* having any appreciable DNA homology with the sequences disclosed in the specification. There was no evidence of record that DNA homologous to OSR-1 from any other nematode was known. The instant specification does not provide any such DNA sequences either. Thus, there is no evidence to record that either Applicant or any one else was in possession of structural information on OSR-1 genes of other nematodes that could be used to mutate them.

The situation here is similar to that of *Regents of the Univ. Calif. v. Eli Lilly & Co.*, 43 USPQ2d 1398 (CA FC, 1997)), which dealt with the adequacy of a description of a nucleotide sequence for a single nucleic acid encoding a protein with a specific activity to provide written description for a genus of nucleic acids that encoded all proteins with that specific activity. The court held that an adequate written description of a nucleic acid requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it, irrespective of the complexity or simplicity of the method; what is required is a description of the nucleic acid itself. It is not sufficient to define DNA or protein solely by its principal biological property, because disclosure of no more than that, as in the instant case, is simply a wish to know the identity of any DNA or protein with that biological property. Naming a type of material generically known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material. When one is unable to envision the detailed constitution of a complex chemical compound having a particular function, such as a nucleic acid, so as to distinguish it from other materials, as well as a method for obtaining it, conception has not been achieved until reduction to practice has occurred, i.e., until after the nucleic acid has been isolated. Thus, claiming all DNA's that achieve a result without defining what means will do so is not in compliance with the description requirement. Rather, it is an attempt to preempt the future before it has arrived. The instant specification identifies two previously characterized genes, *age-1* and *daf-16*, of *C. elegans* that when mutated alter the sensitivity of the nematode to hyper-osmotic stress, and newly characterizes the *osr-1* gene that when mutated decreases sensitivity to hyper-osmotic stress. It is not possible at the present time to envision the complete structure of such a nematode, as it is possible with a specific nucleic acid. In the case of loss-of-

Art Unit: 1633

function mutations, such as in the *age-1*, *daf-16*, and *osr-1* genes, one can envision from the sequence the structure of a suitable mutation, i.e. one that inactivates the gene. One cannot envision gain-of-function mutations, a mutation that changes the function of the gene and its product, without the sequence of the mutation that confers the phenotype. The specification describes generally how mutant nematodes may be isolated, but without either the structure of the wild-type gene, in the case of loss-of-function mutations, or the specific mutated gene, in the case of gain-of-function mutations, one cannot envision the nematode. A nematode that is uncharacterized with respect to its genotype, such as the *osr-2*, *osr-3*, and *osr-4* mutants mentioned in the specification, would be adequately described by biological deposit. However, the specification does not provide evidence of any biological deposits having been made, nor does it mention any specific *osr-2*, *osr-3*, and *osr-4* mutants that could be deposited. Consequently, the instant specification fails to adequately describe the generic invention being claimed for reasons similar to those set forth in *Regents of the Univ. Calif. v. Eli Lilly & Co.*

Claim 12 is directed to siRNA that targets a generic *osr-1* gene or a vector encoding such an siRNA. The specification discloses (page 60, lines 12-16) that the structure of an siRNA must be identical in sequence to its target mRNA, a single mismatch being sufficient to prevent targeting. Thus, in order to envision an siRNA required by the claim, one must either know the sequence of the siRNA or the sequence of the target gene sequence or mRNA sequence. The specification provides sequence information only for the cDNA of the *C. elegans osr-1* gene, and the prior art does not disclose the *osr-1* gene of any nematode. Thus, one cannot envision the siRNA that target other species of *osr-1* genes. There is no evidence of record that Applicant was in possession of any other species of siRNA than that which targets the *C. elegans* gene. Such a

Art Unit: 1633

disclosure is not adequate to describe the genus of nucleic acid embraced by the claim for the same reasons as set forth in *Regents of the Univ. Calif. v. Eli Lilly & Co.*

Claims 6-11 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The claims are directed to a method for treating an unspecified host organism, such as an unspecified plant or animal, with a collection of isolated mutant nematodes altered to reduce or increase sensitivity to desiccation stress. The claims do not recite any particular purpose for administering the nematodes to either a plant or animal. The only uses mentioned in the specification are administration of OSR-1 mutants to host organisms to displace pathogenic versions or sprayed on crops to reduce unspecified pests. The specification provides no more guidance on this method, and provides no working examples of the method.

It is well known in the art, as mentioned at page 2 of the specification, that entomophagic nematodes, such as those of the genera recited in claim 9, are used to as an insecticide to protect plants from insect pests in agriculture and gardening. The specification teaches that mutant Steinernematidae and Heterorhabditidae should have decreased sensitivity to desiccation stress. However, the specification does not describe any such mutant nematodes.

With respect to the second method, the specification teaches that the mutant nematodes should be more sensitive to desiccation stress. The specification does not mention the host organisms this would be practiced on nor the types of nematodes it would be practiced with,

Art Unit: 1633

much less describe the mutant nematodes required. There is no evidence of record that such nematodes have ever been made, much less one determined to be non-pathogenic, have reduced pathogenicity, or be able to displace a wild-type pathogenic nematode infecting a host. If as the specification teaches (page 1 to page 2), resistance to desiccation plays a key role in parasitic nematode epidemiology, then a mutation that lowered desiccation resistance would either confer no competitive advantage over wild-type or would confer a competitive disadvantage, i.e. it would not displace wild-type. There is no evidence of record of any such method in the prior art.

The specification describes a few *C. elegans* mutants with increased or decreased sensitivity to osmotic stress, not desiccation stress, but does not teach administering these to a host organism for any purpose.

A patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion. Tossing out the germ of an idea does not constitute an enabling disclosure. While every aspect of a generic claim need not have been carried out by an inventor, or exemplified in the specification, reasonable detail must be provided in order to enable the skilled artisan to understand and carry out the invention. It is true that a specification need not disclose what is well known in the art. However, that general, oft-repeated statement is merely a rule of supplementation, not a substitute for a basic enabling disclosure. It means that the omission of minor details does not cause a specification to fail to meet the enablement requirement under 35 USC 112, first paragraph. When there is no disclosure of the specific starting materials or conditions under which the process can be carried out, there is a failure to meet the enablement requirement. See *Genentech Inc. v. Novo Nordisk A/S*, 42 USPQ2d 1001, 1005 (Fed. Cir. 1997). That is the case here with respect to the claimed methods.

Due to the virtually complete lack of guidance as to the nematodes, the host organisms and the actual process steps involved in the methods being claimed, undue experimentation would clearly be required in order to practice the claimed invention.

Claims 1-12 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1 and 6 (and their dependent claims) recite "mutant nematodes altered to reduce or increase sensitivity to desiccation stress." As written, it is unclear if there is any relationship between "mutant" and "altered" in this phrase. It is unclear if act of altering is conducted on a mutant nematode, i.e. the mutation in the nematode is not the alteration, or if it produces the mutant nematode, i.e. the mutation in the mutant nematode is the alteration. Also, the terms "reduce" and "increase" are relative terms which renders the claim indefinite. The terms "reduce" and "increase" are not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree. The standard, e.g. a reference nematode, to which the mutant is compared to determine whether it has reduced or increased stress desiccation stress resistance is not recited in claims or described in the specification. Thus, one of ordinary skill in the art would not be reasonably apprised of the scope of the invention.

A broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. See MPEP § 2173.05(c). Note the explanation given by the Board of Patent Appeals and Interferences in *Ex parte Wu*, 10 USPQ2d 2031, 2033 (Bd. Pat. App. & Inter. 1989), as to where broad language is

Art Unit: 1633

followed by "such as" and then narrow language. The Board stated that this can render a claim indefinite by raising a question or doubt as to whether the feature introduced by such language is (a) merely exemplary of the remainder of the claim, and therefore not required, or (b) a required feature of the claims. Note also, for example, the decisions of *Ex parte Steigewald*, 131 USPQ 74 (Bd. App. 1961); *Ex parte Hall*, 83 USPQ 38 (Bd. App. 1948); and *Ex parte Hasche*, 86 USPQ 481 (Bd. App. 1949). In the present instance, claim 2 recites the broad recitation "osmotic stress resistant", and the claim also recites "OSR-1" which is the narrower statement of the range/limitation.

Claim Rejections - 35 USC § 102 & 103

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out

Art Unit: 1633

the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 3-6, 8-10 are rejected under 35 U.S.C. 102(b) as being anticipated by Piggott et al. (Nematol. 2(5): 561-566, 2000).

Piggott discloses a composition comprising *Heterorhabditis megidis* mutant (14), which is a desiccation resistant mutant of wild-type *H. megidis* (UK211). Piggott discloses administering the mutant to late instar larvae of the wax-moth *Galleria mellonella*, an animal. See entire reference, especially page 562, col. 2.

Claims 1 and 3-5 are rejected under 35 U.S.C. 102(b) as being anticipated by Ogg et al. (Nature 389: 994-999, Oct. 1997) as evidenced by the instant specification.

Ogg discloses compositions of mutant *Caenorhabditis elegans daf-16(mgDf50)* (page 995, Table 1). Ogg does not disclose whether this strain of *C. elegans* are desiccation resistant or sensitive. However, the instant specification (e.g. page 6, lines 11-12) discloses that the *daf-16* mutation causes sensitivity to desiccation in comparison to wild-type. With respect to claims 3-5, the limitation of configuring the collection for administration to a host, whether animal or plant, is an intended use of the claimed composition, and the claims recite no particular physical limitation involved in such configuration nor does the specification describe any physical limitations that would distinguish the compositions of Ogg from the claimed composition

Art Unit: 1633

configured for administration. It is submitted that the compositions of Ogg could be administered to a plant or animal host.

Claims 1, 3-6, 8-10 are rejected under 35 U.S.C. 102(b) as being anticipated by O'Leary et al. (Fundam. Appl. Nematol. 20(2): 197-205, 1997).

Claims 6 and 7 are rejected under 35 U.S.C. 103(a) as being unpatentable over O'Leary et al. (Fund. Appl. Nematol. 20(2): 197-205, 1997).

O'Leary discloses compositions comprising *Heterorhabditis megidis* mutants (14), which are desiccation resistant mutants of wild-type *H. megidis* (UK211). O'Leary discloses administering the mutants as third stage infective juveniles to larvae of *Tenebrio molitor* (yellow mealworm) and *Galleria mellonella* (wax-moth), both animals. The mutants showed the same host finding ability and tolerance of temperature range as the wild-type. In addition to having higher desiccation resistance than wild type, the mutants showed higher infectivity and caused greater host mortality than wild-type. Thus, the compositions and methods of treating insects of O'Leary anticipate claims 1, 3-6, and 8-10. See entire document, especially page 198, col. 2; page 199, col. 1; page 201, col. 2 to page 202, col. 1; page 203, col. 2.

With respect to claim 7 (and claim 6 as it embraces the subject matter of claim 7), O'Leary does not explicitly teach administering compositions comprising the mutant nematodes to plants.

However, O'Leary discloses that entomophagic nematodes, such as *H. megidis*, are important biological control agents of soil borne insect pests, but are susceptible to inactivation by evaporative desiccation. This susceptibility limits their usefulness for control of insects pests

Art Unit: 1633

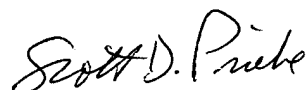
in the soil, and even more so for foliar application (treatment of plants), and poses problems for storage. O'Leary then teaches that the development of strains with infective juveniles having increased desiccation resistance would be desirable for both foliar application and storage.

Therefore, it would have been obvious to use the desiccation tolerant mutants of O'Leary as a replacement for wild type *H. megidis* for foliar treatment for insect pests because O'Leary taught that desiccation tolerance would be desirable in such application, and because the mutants are also more infective of and lethal to the insect pests than is wild-type.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Scott D. Priebe, Ph.D. whose telephone number is (571) 272-0733. The examiner can normally be reached on M-F, 8:00-4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dave Nguyen can be reached on (571) 272-0731. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Scott D. Priebe, Ph.D.
Primary Examiner
Art Unit 1633